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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/818,534	03/14/1997	WILFRED H. NELSON	3922	9647

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HINES, JANA A

ART UNIT	PAPER NUMBER
1645	34

DATE MAILED: 11/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/818,534	NELSON ET AL.	
	Examiner Ja-Na A Hines	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 13 August 2002.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 2 and 9-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 2 and 9-16 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Amendment Entry

1. Amendments have been entered as filed on August 13, 2002. Claims 9 and 11-12 have been amended. Claim 16 has been newly added. Claims 2 and 9-16 are pending in this office action.

Drawings

2. Applicant is required to submit a proposed drawing correction in reply to this Office action. The drawings filed on March 14, 1997 are unacceptable subject to correction of the informalities indicated on the attached "Notice of Draftperson's Patent Drawing Review," PTO-948. In order to avoid abandonment of this application, correction is required in reply to the Office action; the correction will not be held in abeyance.

Response to Arguments

3. Applicant's arguments filed August 13, 2002 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. The rejection of claims 2 and 9-16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention is maintained. Despite applicants amendment, the phrase "when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganism in the sample exist" in the claims is a relative phrase which renders the claim indefinite. The phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Because one could not know whether there was at least a 200:1 ratio of immobilized antibodies to microorganism, unless one knew how many microorganisms were present in the sample and one would not know how many microorganisms were present in the sample before the method of detection was performed, thus the term is relative. The metes and bounds of the phrase cannot be readily determined and the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The rejection of claims 12 and 14-16 under 35 U.S.C. 102(b) as being anticipated by Nelson et al., (US Patent 08/818,534) is maintained for reasons already of record.

Nelson et al., teach the use of backscattered energy i.e., resonance enhanced Raman scattering from a microorganism which exhibits characteristic spectra of that microorganism. Nelson et al., teach the use of a Raman detector and Spex Datamate

microcomputer to display general data acquisition. Therefore, Nelson et al., also teach a system comprising a Raman detector in communication with a display.

Applicants argue that Nelson et al., do not clearly disclose the limitation of a means for contacting the sample with a medium comprising solid phase immobilized antibodies.

However, it is the examiner's position that Nelson et al., teach a system for detecting the presence of a specific microorganism in a sample having a means for contact the sample with a medium; a means for irradiating; and a means for comparing the induced spectrum to detect the presence of the microorganism. Nelson et al., show a slide wherein sample is contained which is means for contacting the sample with a medium. Again it is noted that there is no requirement for the presence of a solid phase comprising immobilized antibodies which specifically bind to a characteristic cell surface antigen on the microorganism to form an antigen-antibody complex. Only the actual components, i.e., the means for contacting said sample with a medium, a means for irradiating and a means for comparing the induced spectrum are considered to have structural limitations. Therefore the means plus function language applicant has intended to set forth is unpersuasive, since only the structural components of the system have patentable weight. There is no structural difference between the claimed invention and the prior art. In order to patentably distinguish the claimed invention from the prior art, there needs to be a structural difference. The prior art structures are capable of performing the intended use and act as a means for contacting, irradiating and comparing, thus the prior art meets the claim limitations.

Thus, Nelson et al., teach a system for detecting the presence of a specific microorganism in a sample comprising a means for contacting the sample with a medium, a means for irradiating and a means for comparison and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The rejection of claims 2, and 9-10 under 35 U.S.C. 103(a) as being unpatentable over Nelson et al. (US 4,487,198) in view of Tarcha et al., (US Patent 5,266,498) is maintained for reasons already of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been *prima facie* obvious to modify the immobilization of the bacteria to a solid surface using polylysine for detecting the presence of specific microorganisms having characteristic resonance enhanced Raman backscattered energy spectrum while using immobilization techniques such as an antibody as taught by Tarcha et al; who teach immobilization of an analyte with antibodies for performing Raman analysis.

Applicants' argument that the effect of the substitution of Nelson et al., in view of Tarcha et al., would have been purely speculative. It is the examiner's position that one would have a reasonable expectation of success by exchanging polylysine immobilization for site-specific immobilized antibody when both techniques are specifically used to immobilize an analyte for Raman analysis and both techniques are known to be compatible with Raman analysis, since Tarcha et al., teach that such binding increases specificity in Raman analysis. Moreover, Tarcha et al., teach antibody immobilization allows the percentage of capture sites available to be up to 75% or more of the number of capture molecules which increases the sensitivity of the assay; therefore one would have had a reasonable expectation of success. Therefore, applicants' argument is unpersuasive

Applicants argue that the method detects a microorganism when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganisms in the sample exist and that the sensitive level of detection is not suggested by the prior art references.

However it is the examiner's position that Tarcha et al., (US Patent 5,266,498) teach the use of Raman light scattering as a means of detecting or measuring the presence of a labeled specific binding member wherein the method teaches assaying an analyte in a test sample by first combining the test sample with a specific binding pair having affinity for the analyte being assayed and the resultant Raman spectra is measured. No more than routine is required to immobilize antibodies in great excess of antigen to increase sensitivity as such techniques are well known in the art. Therefore, such limitation does not obviate the rejection. Moreover, it is noted that one could not know whether at least 200:1 ratio of immobilized antibodies to microorganism was used

unless one knew how many microorganisms were present in the sample and one would not know how many microorganisms were present in the sample before the method of detection was performed.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The instant rejection only takes into account knowledge known in the art at the time of applicants' invention. In this case it would have been prima facie obvious to one of skill in the art to use Raman light scattering as a means of detecting or measuring the presence of a labeled specific binding member wherein the method teaches assaying an analyte in a test sample by first combining the test sample with a specific binding pair having affinity for the analyte being assayed and the resultant Raman spectra is measured. It would have been prima facie obvious to modify the immobilization of the bacteria to a solid surface using polylysine for detecting the presence of specific microorganisms having characteristic resonance enhanced Raman backscattered energy spectrum while using immobilization techniques such as an antibody as taught by Tarcha et al; who teach immobilization of an analyte with antibodies for performing Raman analysis. Moreover, no more than routine is required to immobilize antibodies in great excess of antigen to increase sensitivity as such techniques are well known in the art.

7. The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over Nelson et al. (US 4,487,198) and Tarcha et al., (US Patent 5,266,498), in further view of Muller (US Patent 5,126,244) is maintained for reasons previously stated. Nelson et al. (US 4,487,198) and Tarcha et al., (US Patent 5,266,498) have been discussed above.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, it would have been *prima facie* obvious to modify Nelson et al., and Tarcha et al., who teach a method for detecting the presence of specific microorganisms, including *E. coli*, having characteristic resonance enhanced Raman backscattered energy spectrum by irradiating nucleic acids using solid phase immobilized antibodies wherein the modification is incorporating antibodies against *E. coli*. One would have a reasonable expectation to incorporate the anti-*E. coli* antibody as taught by Muller et al., when the prior art already teach using antibodies to immobilize analyte microorganisms and the prior art teach subjecting *E. coli* to Raman analysis. Moreover, Muller et al., teach qualitative determination of *E. coli* antigens using antibodies that specifically bind to *E. coli*. Therefore, the rejection is maintained.

8. The rejection of claims 2, and 9-10 under 35 U.S.C. 103(a) as being unpatentable over Nelson et al. (US 4,487,198) in view of Tarcha et al., (US Patent 5,266,498) is maintained for reasons already of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, it would have been prima facie obvious to modify the immobilization of bacteria to a solid surface using polylysine for detecting the presence of specific microorganisms having characteristic resonance enhanced Raman backscattered energy spectrum as taught by Chadha et al., who also teach the benefits of: washing cells; using nucleic acids as markers because they show strong resonance enhanced vibrational modes; providing better signals over interference found in Raman spectroscopy; and using the exact same wavelengths separately. Chadha et al., also teach: using 242nm which promises better signal to noise even if Raman cross sections are lower; using 257nm which contains several strong resonance enhanced vibrational modes due to nucleic acids; and using wavelengths of 242, 252, 257nm that are selectively excited for the vibrational modes of various nucleosides and nucleic acids.

One would expect reasonable success by exchanging polylysine immobilization for site-specific immobilized antibodies when both techniques are specifically used to immobilize an analyte for Raman analysis and both techniques are known to be compatible with Raman analysis, when Tarcha et al., teach employing immobilized antibodies that would increase the sensitivity of the assay while such binding increases specificity in Raman analysis. Moreover, Tarcha et al., teach antibodies can be used

with Raman analysis to provide microorganism specific analysis and antibody immobilization allows the percentage of capture sites available to be up to 75% or more of the number of capture molecules which increases the sensitivity of the assay. Therefore, the rejection is maintained.

9. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

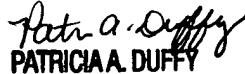
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Art Unit: 1645

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines 
October 24, 2002


PATRICIA A. DUFFY
PRIMARY EXAMINER